Eicosanoids

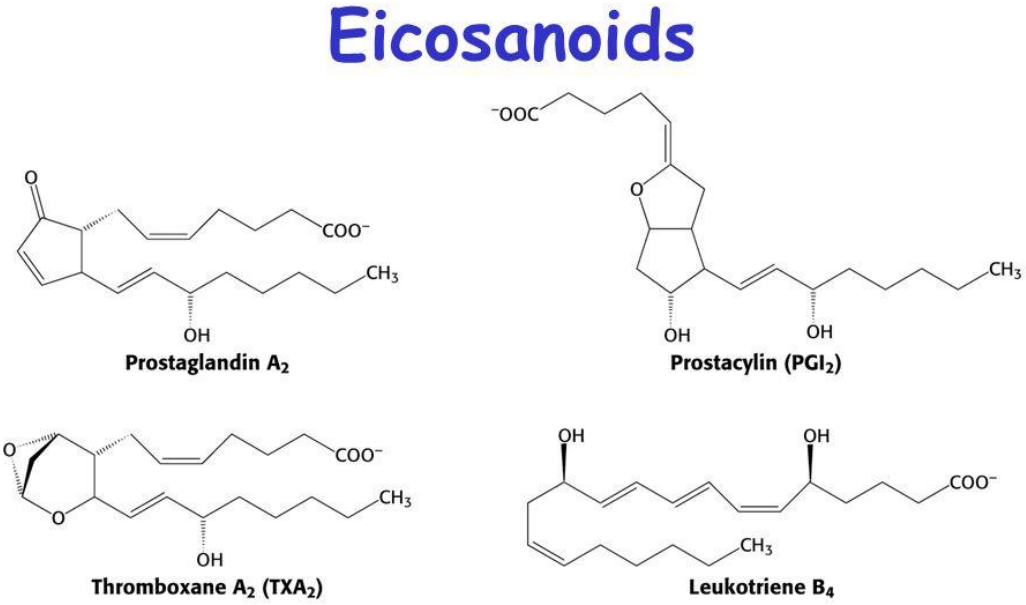
Introduction

- Eicosanoids (eicosa- in Greek: twenty) are special lipid molecules that are derived from arachidonic acid and some other (C20) polyunsaturated fatty acids.
- Physiologically and pharmacologically active compounds
- They include:

♣ Prostanoids which are prostaglandins (PG), prostacyclins (PGI) and thromboxanes (TX).

♣ leukotrienes (LT).

Physiologically, they are considered to act as local hormones functioning through G-protein–linked receptors to elicit their biochemical effects.

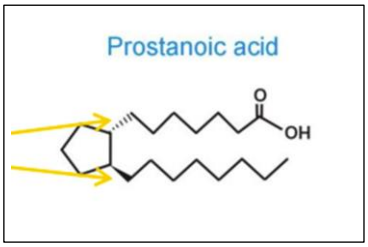


Prostaglandins

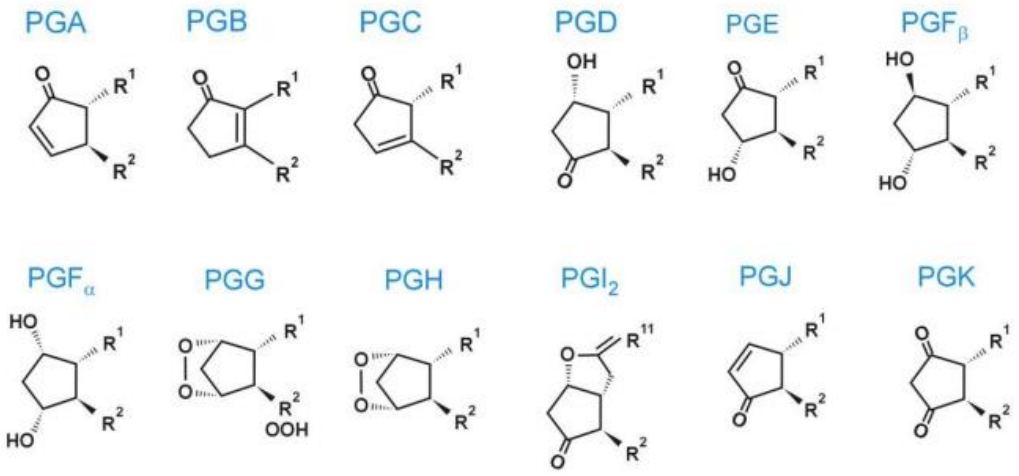
- Origin of the name : Prostaglandins were first discovered in seminal fluid in 1930s when it was observed that fatty acid-derived molecules in the seminal plasma could cause contraction or relaxation of smooth muscles and were thought to be derived from prostate gland , hence the name prostaglandins.
- Prostaglandins have a hormonal like action.
- They are extremely potent compounds that elicit a wide range of responses, both physiologic (inflammatory response) and pathologic (hypersensitivity).

Eicosanoid structure and nomenclature:

- Nomenclature of prostanoids
  - Theoretically from prostanoic acid structure
  - 20 C structure
  - cyclopentane ring
  - substituents are added trans- on adjacent carbons

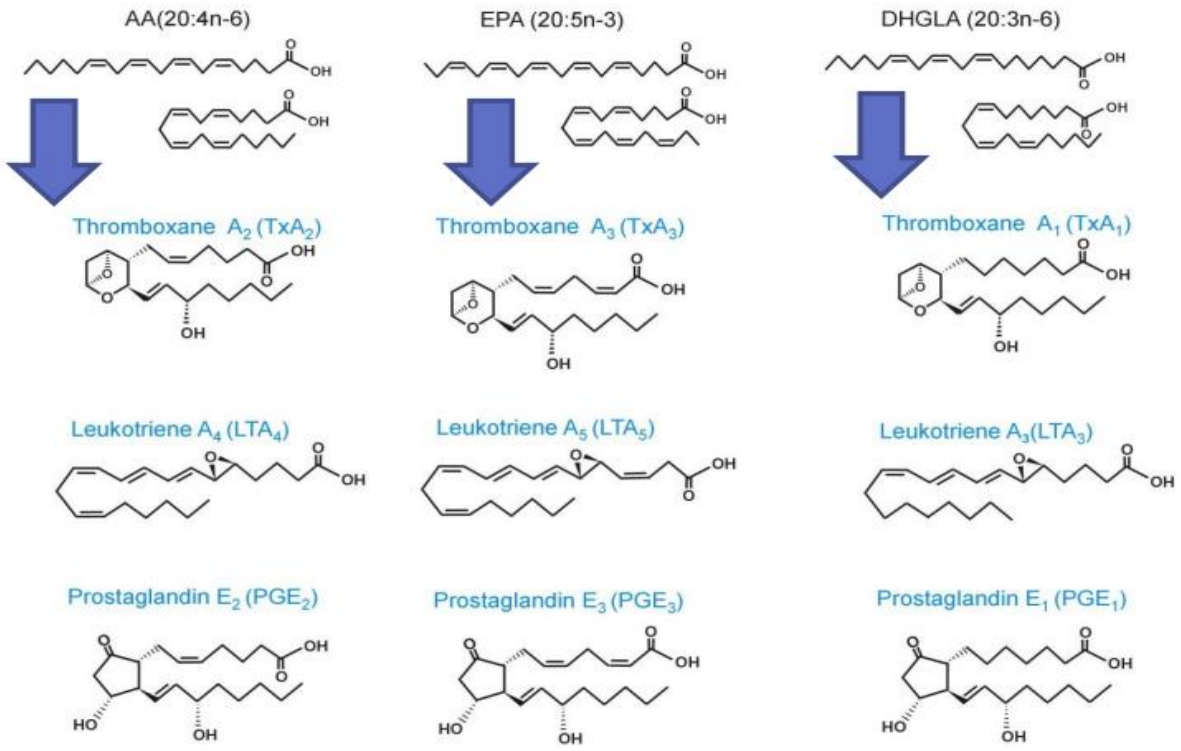


1. Type of ring structure (the third letter)



- They are divided into groups (A to– J) depending on the substitutions on the cyclopentane ring

2. Number of double bonds presents (the number)



Eicosanoids synthesis:

Arachidonic acid is oxygenated by:

- The cyclooxygenase (COX)
- Lipoxygenase (LOX)
- Source of arachidonic acid:
- Arachidonic acid is derived from the C2 position of phospholipids, as a result of phospholipase A2 activity.
- In the first reaction, catalyzed by cyclooxygenase (COX) (also called prostaglandin H synthase), an enzyme that has two activities, a cyclooxygenase and peroxidase, two molecules of

O2 are consumed. COX is present as two isoenzymes, COX-1 and COX-2. The product, an endoperoxide (PGH), is converted to prostaglandins D and E as well as to a thromboxane (TXA2) and prostacyclin (PGI2).

- Prostanoids are synthesized by many different cell types, but each one produces only one type of prostanoid
- **Inhibitors of eicosanoid synthesis:**

- Phospholipase A2 is inhibited by corticosteroids which are thus potent anti-inflammatory agents.

Importance of prostaglandins:

- PGs are potent biologically active substances.
- As little as 1 ng / ml of a certain PG can cause contraction of smooth muscles in animals.
- PGs are involved in a wide variety of conditions.

1. They can increase capillary permeability during inflammatory response and contribute to prolonged erythema, swelling and oedema as well as production of pain.

2. During pregnancy, they are produced in response to oxytocin and promote uterine contraction. Therefore, PGs have been used in termination of pregnancy, in induction of labor, and in prevention of pregnancy. This is by enhancing muscular contraction.

3. In the temperature regulating center of the hypothalamus, the PG synthesis and release is activated by pyrogens leading to production of fever. Aspirin is an antipyretic drug by virtue of its ability to inhibit PG synthesis.

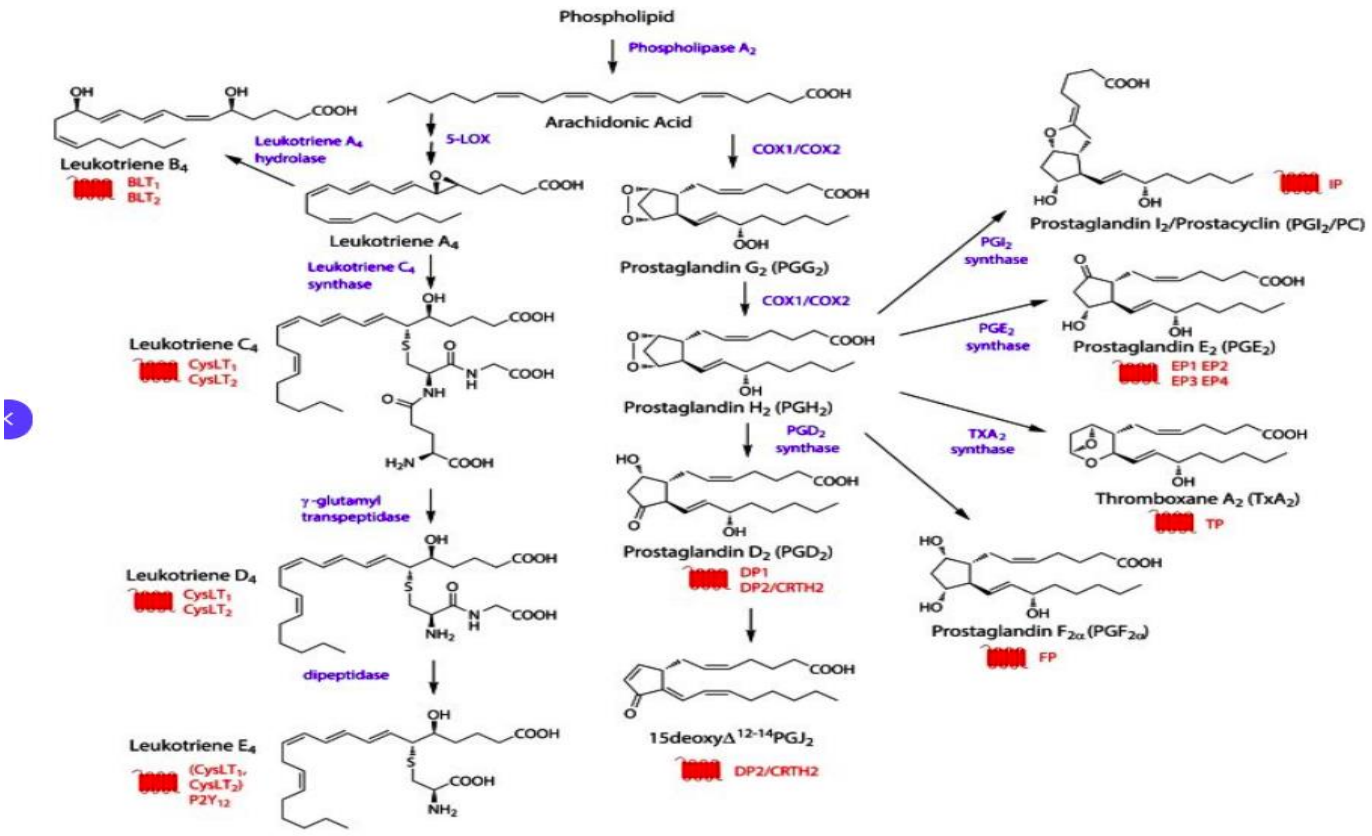
4. PGs inhibit HCl secretion & promote mucus secretion in the stomach and therefore; the inhibition of PG synthesis by some analgesics

(NSAIDs; non-steroidal anti-inflammatory drugs) will increase HCl secretion and at the same time inhibits the formation of the protective mucus. This may cause damage to the gastric mucosa.

Thromboxanes

- Biologically Active Substances Thromboxanes are synthesized in platelets and on release cause vasoconstriction and platelet aggregation.
- Their synthesis is specifically inhibited by low-dose aspirin.

- Prostacyclins (PGI2) are produced by blood vessel walls and are potent inhibitors of platelet aggregation. Thus, thromboxanes and prostacyclins are antagonistic.



- **Leukotrienes (LK):**
  - These are conjugated trienes that are formed from eicosanoic acids in leucocytes, mast cells, platelets and macrophages in response to both immunologic and non-immunologic stimuli.

  - LK synthesis: Their pathway of synthesis is called the lipooxygenase (LOXs) pathway.

REFRANCES

Harper's Biochemistry. Lange, USA.